

AMENDMENTS TO THE CLAIMS

Amendments to the claims are shown below with insertions indicated by underlining and deletions indicated by strikethrough or double bracketing.

1-34. (Canceled)

35. (Currently amended) A method of ~~modulating~~ upmodulating adaptive immune response comprising:

contacting a lymphocyte with an anti-PD-1 antibody, wherein the antibody comprises:
a VH domain or an antigen-binding fragment thereof that comprises 3 CDRs; and a VL domain or an antigen-binding fragment thereof that comprises 3 CDRs;

wherein the antibody comprises at least 3 VH domain CDRs having sequences of:
~~the amino acid sequence as set out in SEQ ID NO:19, SEQ ID NO:25, SEQ ID NO:31, SEQ ID NO:37 or SEQ ID NO:52~~

SEQ ID NO:23, SEQ ID NO:24 and SEQ ID NO:25; or

SEQ ID NO:29, SEQ ID NO:30 and SEQ ID NO:31; or

SEQ ID NO:35, SEQ ID NO:36 and SEQ ID NO:37;

or at least 3 VL domain CDRs having sequences of:

SEQ ID NO:26, SEQ ID NO:27 and SEQ ID NO:28; or

SEQ ID NO:32, SEQ ID NO:33 and SEQ ID NO:34; or

SEQ ID NO:38, SEQ ID NO:39 and SEQ ID NO:40.

36. (Currently amended) The method of claim 35, wherein the antibody comprises a VH domain ~~an amino acid sequence~~ selected from the group consisting of ~~SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, and SEQ ID NO:14; [[,]]~~ or a VL domain selected from the group consisting of SEQ IS NO: 8, SEQ ID NO: 12 and SEQ ID NO:16[[,]] ~~SEQ ID NO:47 and SEQ ID NO:49.~~

37. (Canceled)

38. (Previously presented) The method of claim 35, wherein the antibody specifically binds to the extracellular domain of PD-1 with an affinity constant greater than 10^7 M^{-1} .

39. (Currently amended) The method of claim 37, where the antibody inhibits the binding of PD-L1 or PD-L2 ~~PD-L~~ to PD-1 with an IC_{50} of less than 10 nM.

40. (Previously presented) The method of claim 35, wherein the antibody is a human antibody.

41. (Previously presented) The method of claim 35, wherein the antibody is IgG_1 or IgG_4 .

42. (Previously presented) The method of claim 41, wherein the antibody is $\text{IgG}_{1\lambda}$ or $\text{IgG}_{1\kappa}$.

43. (Currently amended) The method of claim 35, wherein the antibody is selected from the group consisting of: PD1-17, PD1-28, PD1-33, PD1-35 or PD1-F2.

an antibody comprising a VH domain of SEQ ID NO:6 and a VL domain of SEQ ID NO: 8;

an antibody comprising a VH domain of SEQ ID NO:10 and a VL domain of SEQ ID NO:

12; and

an antibody comprising a VH domain of SEQ ID NO:14 and a VL domain of SEQ ID NO:

16.

44. (Previously presented) The method of claim 35, wherein the lymphocyte is a T cell, B cell or monocyte.

45. (Canceled)

46. (Previously presented) The method of claim 35, wherein the antibody is immobilized on a support matrix or crosslinked.
47. (Previously presented) The method of claim 35, wherein the support matrix comprises one or more material chosen from agarose, dextran, cellulose, PVDF, silica, nylon, dacron, polystyrene, polyacrylates, polyvinyls, teflons, polyglycolic acid, polyhydroxyalkanoate, collagen and gelatin.
48. (Previously presented) The method of claim 35, wherein the anti-PD-1 antibody modulates immune cell response mediated by an antigen receptor.
49. (Previously presented) The method of claim 48, wherein the antigen receptor signal is co-presented with the anti-PD-1 antibody.
50. (Previously presented) The method of claim 48, wherein the antigen receptor signal and anti-PD-1 antibody are spaced by no more than 100 μm .
51. (Previously presented) The method of claim 48, wherein the antigen receptor signal is delivered by an anti-CD3 antibody.